is independent of integration[,] or level of expression[~~, or transcription~~] of the delivered nucleic acid composition.

Claims 12-13 **(cancelled)**

14. (currently amended) A method according to claim 11, wherein the first sequence of muting nucleic acid composition is DNA[~~, further comprising the step of engineering the DNA into a recombinant vector before the delivering step~~].

Claims 15-27 **(cancelled)**

28. **(withdrawn)** A method for identifying a muting nucleic acid that reduces expression of an endogenous target gene having unwanted activity in cells of an animal, comprising the steps of:

(a) providing a set of fragments of DNA encoding the target gene, wherein the fragments are engineered into a plurality of vector molecules to produce a recombinant vector library;

(b) delivering the vector library into the cells, to form a plurality of transgenic cloned fragment recipients; and

(c) comparing expression of the target gene in each of a subset of the cloned recipients, to expression of the target gene in the cells of the animal, to identify a cloned recipient having a vector with the muting nucleic acid, wherein expression of the target gene is reduced.

29. **(withdrawn)** A method according to claim 28, wherein the animal is warm-blooded.

30. **(withdrawn)** A method according to claim 29, wherein the animal is a mammal.

31. (**withdrawn**) A method according to claim 28, wherein the vector carries also a chemical resistance gene conferring a phenotype which is ability to grow in the presence of the chemical.

32. (**withdrawn**) A method according to claim 31, having an additional step of:

(a) comparing expression of the resistance gene in the cell having the muting nucleic acid, with expression of the resistance gene in the animal cell.

33. (**withdrawn**) A method according to claim 32, wherein the resistance gene is selected from the group consisting of *AMP* and *CAT*, encoding encoding β-lactamase and chloramphenicol acetyl transferase, respectively.

34. (**withdrawn**) A method according to claim 28, having a further step:

(a) comparing expression of a second endogenous gene which is not the target gene in the cell having a muting nucleic acid, with expression of the second endogenous gene in the animal cell.

35. (**withdrawn**) A method according to claim 34, wherein the second endogenous gene is *GADPH*, encoding glyceraldehyde-3-phosphate dehydrogenase.

36. (**withdrawn**) A method of evaluating a phenotype of animal cells engineered to mute expression of a target endogenous gene, comprising:

(a) transforming animal cells capable of expressing the target gene with the vector having the muting nucleic acid obtained according to the method of claim 28; and

(b) observing the transformed cells for an altered phenotype in comparison to the parental animal cells capable of expressing the target gene.

37. (**withdrawn**) A method according to claim 36, wherein the altered phenotype under a set of specified conditions is selected from the group consisting of an alteration of: growth rate, nutritional requirement, contact inhibition among confluent cells, formation of foci, presence of a receptor for a ligand, signal transduction in response to an effector molecule, sensitivity to a pathogen, expression of a developmental protein, and cell cycle pattern.

38. (**withdrawn**) A method according to claim 37, wherein the altered phenotype is cessation of growth or colony formation under specified conditions different from the conditions for growth of the parental animal cells capable of expressing the target gene.

39. (**withdrawn**) A method according to claim 37, wherein the specified conditions different from the conditions for growth of the parental animal cells capable of expressing the target gene comprise at least one of the conditions selected from the group of: an elevated temperature, a depressed temperature, a decreased serum concentration, an elevated serum concentration, a decreased carbon dioxide concentration, an increased carbon dioxide concentration, an increased density of plating, and a decreased density of plating.

40. (**withdrawn**) A method according to claim 37, wherein the altered phenotype is cessation of growth or colony formation under specified conditions that are the same as the conditions for growth of the parental animal cells capable of expressing the target gene.

41. (**withdrawn**) A method according to claim 37, wherein the animal cells are present in an embryonic or postnatal animal.

42. (**withdrawn**) A method of screening a plurality of molecules to obtain a composition capable of muting expression of an endogenous gene in cells of a cell line, comprising:

mixing a subset of each of the plurality of molecules with a plurality of samples of the cells, to produce a plurality of test cell cultures;

providing a nucleic acid capable of muting expression of the gene;

transforming the nucleic acid into a sample of the cells, to produce a positive control cell culture having muting of expression of the endogenous gene; and

detecting an amount of expression of the endogenous gene in each of the test cell cultures in comparison with the positive control cell culture and with untreated cells of the cell line, such that a test cell culture with substantially reduced expression of the gene compared to expression in the untreated cells, and substantially equivalent expression compared to cells in the positive control culture, identifies the composition capable of muting expression of the gene.

43. (**withdrawn**) A method according to claim 42, wherein detecting expression of the endogenous gene comprises analyzing cell RNA by hybridization with a probe.

44. (**withdrawn**) A method according to claim 43, wherein the hybrid of the cell RNA and the probe is digested with RNase.

45. (**withdrawn**) A method according to claim 44, the digested RNA is submitted to gel electrophoresis to determine the size of the cell RNA protected from RNase digestion by the probe.

46. (**withdrawn**) A method according to claim 42, wherein detecting expression of the endogenous gene comprises detecting a color change or absence of a color change in the cells.

47. (**withdrawn**) A method according to claim 46, wherein the color change in the cells is indicative of expression of the endogenous gene which has been fused to a second gene having a colorimetric assay.

48. (**withdrawn**) A method according to claim 42, wherein the molecules are selected from the group consisting of extracts of natural product fermentations and synthesized organic chemicals.

49. (**withdrawn**) A method according to claim 48, wherein the organic chemicals are synthesized according to combinatorial methods.

Claim 50 (**cancelled**)

51. (**withdrawn**) A method of screening a plurality of molecules to obtain a composition capable of alleviating muting of expression of an endogenous gene in cells of a cell line having a muted endogenous gene, comprising:

mixing a subset of each of the plurality of molecules with a plurality of samples of the cells having the muted endogenous gene, to produce a plurality of test cell cultures; and

detecting amounts of expression of the endogenous gene in each of the test cell cultures in comparison with the cells of the cell line having the muted endogenous gene, and in untreated cells of a parental cell line in which the endogenous gene is not muted, such that a test cell culture with expression of the gene that is substantially greater than the expression in the cell line having the muted endogenous gene, and that is substantially equivalent to expression in cells of the parental non-muted culture, identifies the composition capable of alleviating muting of expression of the gene.

Claim 52 (**cancelled**)

53. (**withdrawn**) A kit for identifying a muting nucleic acid that reduces expression of an endogenous gene, the kit comprising reagents for assaying quantitatively both protection of a riboprobe from ribonuclease digestion, and amount of transfected DNA.

54. (**withdrawn**) A kit according to claim 53, wherein the reagents comprise chemicals, stabilized enzymes, and buffers.

55. (**withdrawn**) A kit according to claim 53, wherein the reagents comprise diethylpyrocarbonate-treated water, placental RNase inhibitor, tRNA, a buffer containing piperazine-*N,N'*-bis(2-ethanesulfonic acid), a DNase I digestion buffer, phenylmethylsulfonyl fluoride, and gelatin.

56. (**withdrawn**) A kit according to claim 54, wherein the stabilized enzymes comprise: an RNA polymerase selected from the group of SP6 RNA polymerase and T7 RNA polymerase; a ribonuclease selected from the group of RNase I and a mixture of RNases A and T_1; *Taq* polymerase; proteinase K; and DNase-free pancreatic RNase.

57. (currently amended) A method for muting expression of an endogenous gene in a cultured population of animal cells, the method comprising:

(a) screening to identify[~~ying~~] a muting nucleic acid composition having a sequence that is homologous to a sequence in the endogenous gene, wherein the gene is one of a collagen, tumor necrosis factor (TNF), *tat*, and an immunoglobulin gene, the nucleic acid composition being double stranded [~~or having the capacity to become double-stranded upon delivery to the population of cells~~], wherein screening to identify[~~ing~~] comprises the steps of:

(i) designating the entire gene sequence as a potential muting nucleic acid composition;

(ii) identifying a first sequence [~~muting fragments~~] of [~~the~~] muting nucleic acid composition homologous to portions of the endogenous gene that mutes at the level of post-transcription;

(b) delivering the first sequence of muting nucleic acid composition into the population of cells; and

(c) muting expression of the endogenous gene [~~wherein muting comprises muting at the level of post-transcription in the population as a whole, and~~] wherein such muting is independent of integration[,]or level of expression[~~, or transcription~~] of the delivered nucleic acid composition.

58. (previously added) A method according to claim 57, wherein the endogenous gene is a type I collagen.

59. (previously added) A method according to claim 58, wherein the endogenous gene is pro-α1(I) collagen.

60. (currently amended) A method according to claim 57, wherein the cultured population of animal cells [~~are~~] is a population of rodent cells.

Claims 61-68. **(cancelled)**

69. (currently amended) A method for muting expression of an endogenous gene in a population of [~~animal~~] rodent cells, the method comprising:

(a) screening to identify[~~ying~~] a muting nucleic acid composition of DNA having a sequence that is homologous to a sequence in the endogenous gene, wherein the gene is [one of] a collagen[, tumor necrosis factor (TNF), *tat*, and an immunoglobulin] gene, the nucleic acid composition being double stranded, and wherein screening to identify[~~ing~~] comprises the steps of:

(i) designating the entire gene sequence as [~~the~~] a potential muting nucleic acid composition;

(ii) identifying a first sequence [~~muting fragments~~] of [~~the~~] muting nucleic acid composition homologous to portions of the endogenous gene that mutes at the level of post-transcription;

(b) delivering the first sequence of muting nucleic acid composition into the population of rodent cells; and

(c) muting expression of the endogenous gene [~~wherein muting comprises muting at the level of post-transcription in the population as a whole, and~~] wherein such muting is independent of integration[,]or level of expression[~~, or transcription~~] of the delivered nucleic acid composition.

70. (new) A method for muting according to claim 11 further comprising:

after identifying a first sequence,

(iii) identifying a second sequence of muting nucleic acid composition that mutes at the level of transcription, wherein the first and second sequence of muting nucleic acid composition may be part of a single nucleic acid composition; and

in the delivering, further comprising:

delivering the second sequence of muting nucleic acid composition into the population of cells.

71. (new) A method for muting according to claim 57 further comprising:

after identifying a first sequence,

(iii) identifying a second sequence of muting nucleic acid composition that mutes at the level of transcription, wherein the first and second sequence of muting nucleic acid composition may be part of a single nucleic acid composition; and

in the delivering, further comprising:

delivering the second sequence of muting nucleic acid composition into the population of cells.

72. (new) A method according to claim 71, wherein the endogenous gene is pro-α1(I) collagen and wherein the first or second sequence of muting nucleic acid composition is homologous to an endogenous sequence comprising a portion of the pro-α1(I) collagen gene selected from at least one of the group of: a 5'-untranscribed portion, a transcribed portion, a 3'-untranslated portion, a 3'-untranscribed portion, and a portion that overlaps adjacent ends of at least two portions of the pro-α1(I) collagen gene.

73. (new) A method according to claim 72, wherein the first or second sequence of muting nucleic acid composition comprises a sequence homologous to an endogenous sequence located in a 5'-portion of the pro-α1(I) collagen gene.

74. (new) A method according to claim 72, wherein the first or second sequence of muting nucleic acid composition comprises a sequence that is homologous to an endogenous sequence located in a 3'-portion of the pro-α1(I) collagen gene including a 3'-untranscribed portion, a 3'-untranslated portion, and a portion that overlaps the 3'-end of a coding portion.

75. (new) A method according to claim 71, wherein delivering the first or second muting sequence of nucleic acid composition is selected from the group of: transforming,

transfecting, electroporating, infecting, or lipofecting as the means for delivering the nucleic acid composition into the cells.

76. (new) A method according to claim 71 wherein the first and second sequence of muting nucleic acid composition is DNA.

77. (new) A method for muting according to claim 69 further comprising:

after identifying a first sequence,

(iii) identifying a second sequence of muting nucleic acid composition of DNA that mutes at the level of transcription, wherein the first and second sequence of muting nucleic acid composition may be part of a single DNA composition; and

in the delivering, further comprising:

delivering the second sequence of muting nucleic acid composition into the population of rodent cells.

78. (new) A method according to claim 77, wherein the endogenous gene is a type I collagen.

79. (new) A method according to claim 78, wherein the endogenous gene is pro-α1(I) collagen.

80. (new) A method for muting expression of an endogenous gene in a cultured population of rodent cells, the method comprising:

(a) screening to identify a muting nucleic acid composition having a sequence that is homologous to a sequence in the endogenous gene, wherein the gene is one of a collagen, tumor necrosis factor (TNF), *tat*, and an immunoglobulin gene, the nucleic acid composition being double stranded, wherein screening to identify comprises the steps of:

(i) designating the entire gene sequence as a potential muting nucleic acid composition;

(ii) identifying a first sequence of muting nucleic acid composition homologous to portions of the endogenous gene that mutes at the level of post-transcription;

(b) delivering the first sequence of muting nucleic acid composition into the population of cells; and

(c) muting expression of the endogenous gene wherein such muting is independent of integration or level of expression of the delivered nucleic acid composition.

81. (new) A method for muting according to claim 80 further comprising:
after identifying a first sequence,

(iii) identifying a second sequence of muting nucleic acid composition that mutes at the level of transcription, wherein the first and second sequences may be part of a single nucleic acid composition; and
in the delivering, further comprising:

delivering the second sequence of muting nucleic acid composition into the population of cells.

82. (new) A method according to claim 81 wherein the first and second sequence of muting nucleic acid composition is DNA.

83. (new) A method according to claim 81, wherein the endogenous gene is a type I collagen.

84. (new) A method according to claim 83, wherein the endogenous gene is pro-α1(I) collagen.